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10/828,919	04/20/2004	Michael J. Adang	UGR-100XD1	6165

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EXAMINER	
LIU, SUE XU	

ART UNIT	PAPER NUMBER
1639	

MAIL DATE	DELIVERY MODE
04/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/828,919	ADANG ET AL.	
	Examiner	Art Unit	
	SUE LIU	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-23,35,36 and 38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-22,35,36 and 38* is/are rejected.

7)☒ Claim(s) *23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

1. Claims 1-19, 24-34 and 37 have been cancelled as filed 11/26/07.

Claim 38 has been added as filed on 11/26/07.

Claims 20-23, 35, 36 and 38 are currently pending.

Claims 20-23, 35, 36 and 38 are being examined in this application.

Election/Restrictions

2. Applicant's election of Group I (claims 20-24, 35 and 36) in the reply filed on 5/11/07 is previously acknowledged.

3. The newly added claim 38 is grouped with the elected Group I invention.

Priority

4. This application appears to be a CONTINUATION of U.S. Patent Application Nos. 09/629,596 (filed 7/31/2000), which is now abandoned (4/21/2004). The '596 application claims priority to U.S. Provisional Patent Application Nos. 60/146,646, filed 7/30/1999.

5. Applicants' statement of "SEQ ID NOS:9 and 10 were provided in Figure 1 of the provisional application" (60/146,646) in the Reply, p.5, para 2, is acknowledged.

Specification

6. Applicants' filed amendment to the instant specification to update the priority data is acknowledged and entered.

Affidavit/Declaration

7. The Affidavit/Declaration of Michael J. Adang, Ph.D. under 37 CFR 1.132 filed on 11/26/07 has been entered and considered. Applicant's (Michael J. Adang) statements regarding the Kasman reference (Declaration, pp.2+) overcomes the rejection under 35 USC 102(a) over the Kasman reference.

8. However, the said Declaration does not overcome the outstanding claim rejections over the Marzari reference under 35 USC 102(b) as well as the outstand claim rejection under 35 USC 103(a) over the combination of Marzari and other references. See the following sections of the instant office action on discussion of the said Declaration.

Claim Objection(s) / Rejection(s) Withdrawn

9. In light of applicants' amendments to the claims and supporting arguments, the following rejection as set forth in the previous office action is withdrawn:

A.) Claims 20-24, 35 and 36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

10. In light of applicant's statement (Declaration) regarding the inventions and the co-authors of the Kasman reference, the following rejection as set forth in the previous office action is withdrawn:

A.) Claims 20-22, 24, 35 and 36 are rejected under **35 U.S.C. 102(a)** as being anticipated by Kasman et al (Applied and Environmental Microbiology. Vol. 64(8): 2995-3003; 8/1998; cited in IDS).

Claim Objection(s) / Rejection(s) Maintained

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(Note: the instant claim numbers are in bold font.)

Marzari

12. Claims 20-22, 35 and 38 are rejected under **35 U.S.C. 102(b)** as being anticipated by Marzari et al (FEBS Letter. Vol. 411: 27-31; 1997; cited in IDS). The previous rejection over claims 20-22 and 35 is maintained for the reasons of record as set forth in the previous Office action as well as the reasons below. The previous rejection over claim 24 is moot due to

applicant's cancellation of the said claim. The rejection over claim 38 is necessitated by applicant's amendment to the claims.

The instant claims recite a phage comprising a fusion protein comprising a Cry toxin and a phage coat protein, wherein said Cry toxin is displayed on the surface of said phage.

Marzari et al, throughout the publication, teach using phage to display Cry toxin protein (Abstract). The reference teaches fusing CryIA(a) toxin with gene III coat protein of phage through molecular cloning techniques (using plasmid DNA constructs), and displaying the fusion protein on the surface of the phage particles (e.g. Abstract; p. 27, col.2, para 3; pp. 27-28, bridging paras), which read on the phage of **clm 20**.

The reference teaches the Cry protein is derived from *Bacillus thuringiensis* (e.g. Abstract), which reads on the product by process limitation of **clm 21**.

The reference teaches the g3p coat protein is from filamentous bacteriophages (e.g. p. 27, col.2, para 3), which reads on the product by process limitation of **clms 22 and 24**.

The reference teaches fusing partial CryIA(a) protein with the phage coat protein (e.g. Figure 1; pp. 27-28, bridging), which reads on the "modification" of **clm 35**.

The reference also teaches displaying sections or fragments of the CryIA toxin (such as BtL and BtS; e.g. pp.28-29; Figure 1), which reads on the truncated Cry toxin of **clm 38**.

Discussion and Answer to Argument

13. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue the Marzari reference does not teach "an active Cry toxin (fused with a phage protein) displayed on the surface of the phage". (Reply, p.6, para 1). Applicants also relied on the "Declaration of Michael J. Adang, Ph.D." for rebuttal of the rejection over Marzari.

Applicants also state the intended use of the claimed phage, which the said intended uses are not features recited in the instant claims (Reply, p.6, para 2-3). In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "active toxin", "screening the phage for binding then toxin activity", or "screen for insecticidal activity of the displayed protein") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Contrary to applicant's assertion, the Marzari reference teaches "a phage comprising a fusion protein comprising a Cry toxin and a phage coat protein" as recited in the instant claims. The term "Cry toxin" is generally used in the art to refer to the bacterial "crystal protein" family, as evidenced by Marzari et al (e.g. Abstract). In addition, the instant specification broadly defines the term "toxin" (activity) as referring "to the ability of a given protein to have an observable effect on pests" (spec. p.3, lines 4+). The "CryIA(a)" protein is an "insecticidal toxin"

as taught by the Marzari reference (e.g. Title and Abstract).The fragments of the CryIA(a) toxin are also encompassed by the broad definition of "toxin" of the instant specification, because the fragments have the abilities to have "an observable effect on pests". That is the CryIA(a) protein or fragments thereof have the capability of having "an observable effect on pests" (such as insecticidal activity or other activities such as growth) without evidence to the contrary.

The "Declaration of Michael J. Adang, Ph.D." states "Marzari actually teaches away from our invention". It is initially noted that the above rejection over the Marzari reference is under 35 USC 102(b). The argument of "teaching away" is not relevant in regard to a rejection under 35 USC 102(b). The Declaration also quoted a passage on page 30 of the Marzari reference to indicate "lack of display". The cited passage is discussing the fully activated large toxin fragments are not well displayed, but the large activated toxin fragments of the toxin are displayed using helper phage (e.g. p.30, col.2, para 2; Figure 2; p.29). The passage also teaches that other fragments of the Cry toxin are also displayed (e.g. p.30, col.2, para 2; Figure 2; p.29). In fact, applicant also acknowledges this teaching in the Declaration (p.2, para 1). Further, the low amount of recombinant Cry toxin observed was mostly due to intolerance of the toxin by the bacteria not the phage particle (e.g. p.30, col.2). That is the bacteria's growth rate was slowed, which caused low phage titres (e.g. Table 1). The reference does NOT teach that the Cry toxin protein or its toxin fragments cannot be displayed on the surface of the phage particle.

The Declaration also states "one could not then use the fragment to screen for insecticidal activity". (p.2, para 3). However, no supporting evidence was provided for this assertion. Further, the recitation of "screen for insecticidal activity" is not a feature recited in the instant claims.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Marzari and Others

15. Claims 20-22, 35, 36 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marzari et al (FEBS Letter. Vol. 411: 27-31; 1997; cited in IDS), in view of Stewart et al (Plant Physiology. Vol. 112: 121-129; 1996; cited in IDS), and if necessary, in view of Masson et al (Journal of Biological Chemistry. Vol. 270(35): 20309-20315; 1995; cited in IDS). The previous rejection over claims 20-22, 35 and 36 is maintained for the reasons of record as set forth in the previous Office action as well as the reasons below. The previous rejection over claim 24 is moot due to applicant's cancellation of the said claim. The rejection over claim 38 is necessitated by applicant's amendment to the claims.

Marzari et al, throughout the publication, teach using phage to display Cry protein, as discussed above.

Marzari et al do not explicitly teach the Cry protein is Cry1Ac, as recited in **clm 36**.

However, Stewart et al, throughout the publication, teach Cry1Ac proteins and its encoding polynucleotide (e.g. Abstract; p. 122, col.1, para 4). The reference also teaches the

advantages of generating DNA vectors comprising Bt toxins such as increased insecticidal efficiency (e.g. p. 121, col.2, para 3).

In addition, Masson et al, throughout the publication, teach various Cry toxins such as Cry1Ac and Cry1Ab. (Abstract). The Masson reference also teaches the advantages of Cry1Ac toxin such as avoiding insect resistance to the toxin. (e.g. p. 20309, col.2, para 1).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to make a phage comprising DNA encoding for the Cry1Ac protein fused to the gIII coat protein of phage.

A person of ordinary skill in the art would have been motivated at the time of the invention to make a phage displaying vector comprising polynucleotides encoding for Cry1Ac protein, because the advantages of using phage displaying technology to study protein mutations as taught by Marzari et al, and the need to generate toxins such as Cry1Ac that would reduce insect resistance, as taught by Masson et al.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since Marzari et al, Stewart et al, and Masson et al have demonstrated the success of making polynucleotides encoding for Cry toxins, and manipulating phage vectors to encompass Cry toxin encoding DNAs.

Discussion and Answer to Argument

16. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants traversed the above rejection with the same argument as the traversal over the Marzari reference. Thus, applicants are respectively directed to the discussion under the Marzari reference for answer to arguments.

In the Declaration, applicants also assert the Marzari reference "teaches away" from the claimed invention by stating "Marzari clearly teach away from using insecticidal fragments of *B.t. Cry* proteins." *[sic]* (Declaration, p.2, para 2)

However, the above cited statement from the "Declaration" is in contradiction to the reference's teachings. The Marzari reference teaches using phage to successfully display both large and small fragments of the Cry toxin proteins as discussed above. (e.g. Marzari, p.30, col.2, para 2; Figure 2; p.29). Applicants also state in the "Declaration" that the Marzari reference teaches displaying fragments of the Cry toxin (Declaration, p.2, para 1). Applicants have not provided any evidence to support the assertion that the fragments of the Marzari reference are "non-toxic". More importantly, applicants have not demonstrated how the Cry protein toxin fragments of the Marzari reference falls outside the broad scope of the term "toxic" as it is defined in the instant specification. In other words, applicants have not demonstrated true structural differences between the Marzari reference and the instant claims.

In addition, the Marzari reference contains statements indicating that the phage displayed Cry toxin fragments can have insecticidal activities. For example, the fact that the displayed fragments were "toxic" to the bacteria host cells (as acknowledged by the applicants) indicate that the said Cry fragments are "toxic" as the term is broadly used in the instant specification. Applicants also seem to state in the "Declaration" that the "loop2 and domain II" regions of the Cry toxin are "non-toxic fragments" (Declaration, p.2, para 2), which is contrary to the direct

teaching of the Marzari reference as well as the teachings of the state of the art. The Marzari reference states "interaction of domain II with the mid-gut receptor [of insects] is considered one of the key factors for insect toxicity and specificity" (Marzari, p.27, left col.). Thus, the phage comprising the Cry fusion protein is structurally the same as the instantly claimed invention, and the reference does not teach away from the instantly claimed phage.

New Claim Objection(s) / Rejection(s)

Claim Rejections - 35 USC § 112

17. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter Rejection

18. Claim 38 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 35 has been added as part of a claim amendment filed on 11/26/07. However, the instant specification does not appear to provide support for the claimed "truncated toxin" recited in Claim 38.

If Applicant believes this rejection is in error, applicant must disclose where in the specification support for the entire scope of the amendment(s) and/or new claims can be found. As a result, Claim 38 represents new matter.

Claim Objections

19. Claim 23 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. This objection is necessitated by applicant's amendments to the claims.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/S. L./
Examiner, Art Unit 1639
4/1/08

/Jon D. Epperson/
Primary Examiner, AU 1639